(5/5/2017)

Find Functions: KEGG Orthology Terms & Pathways

From the **Find Function** top-level menu, the **KEGG** option on the second-level menu leads to the **KEGG Orthology Terms and Pathways** browser, as shown in Figure 1(i). KEGG Orthology (KO) terms identify orthologous groups of genes organized using the BRITE functional hierarchy (http://www.genome.jp/kegg/brite.html - see Figure 1(ii)).

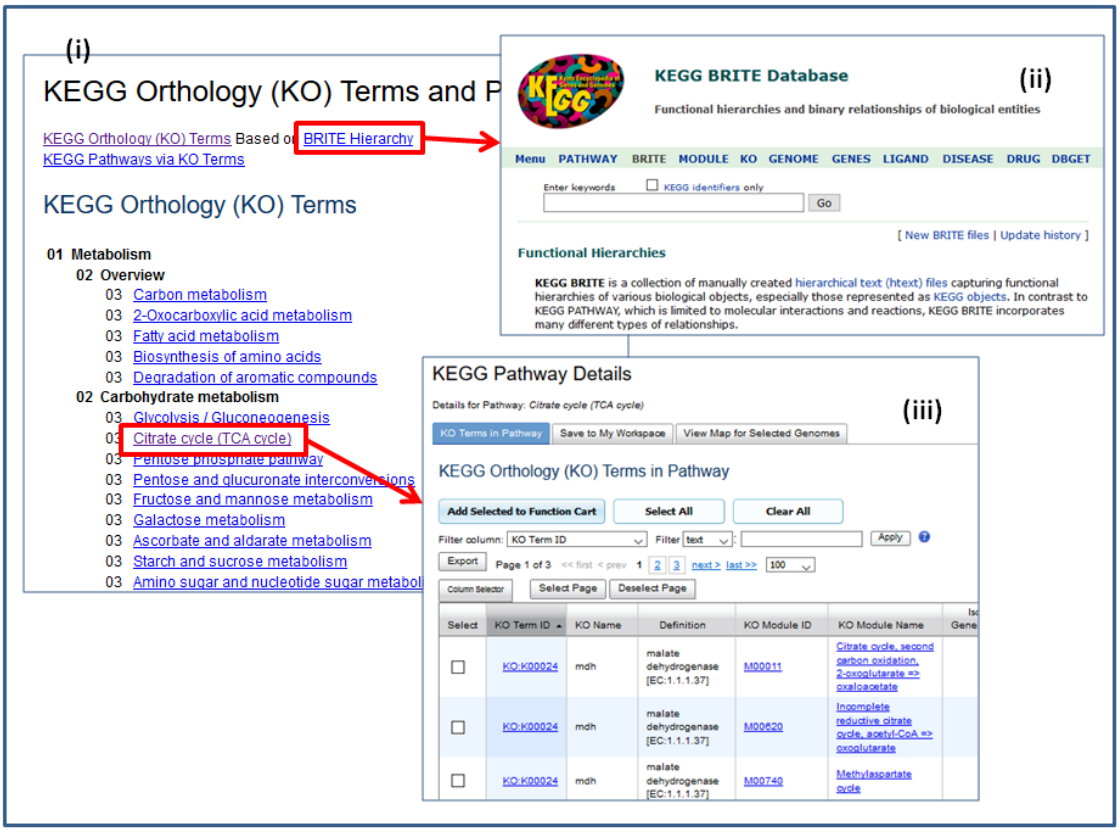

Figure 1. KEGG Orthology Terms and Pathways

Clicking on any pathway names shown in Figure 1(i) will lead to a **KEGG Pathway Details** page as shown in Figure 1(iii) with all the KO terms associated with this pathway listed in a table display. Users can select a subset of the KO terms to be added to the Function Cart or Workspace (in the **Save to My Workspace** tab) for further analysis.

The **View Map for Selected Genomes** tab in the KEGG Pathway Details page (Figure 1(iii)) allows users to view how genes of selected genomes are mapped to the functions in this pathway. For example, select to add *Acidianus hospitalis W1* (in Figure 2(i)) and then click the "View Map" button to lead to a KEGG map display highlighted with functions associated with genes of this genome (Figure 2(ii)). To see the actual gene list (Figure 2(iii)), select the colored EC number square on the KEGG map.

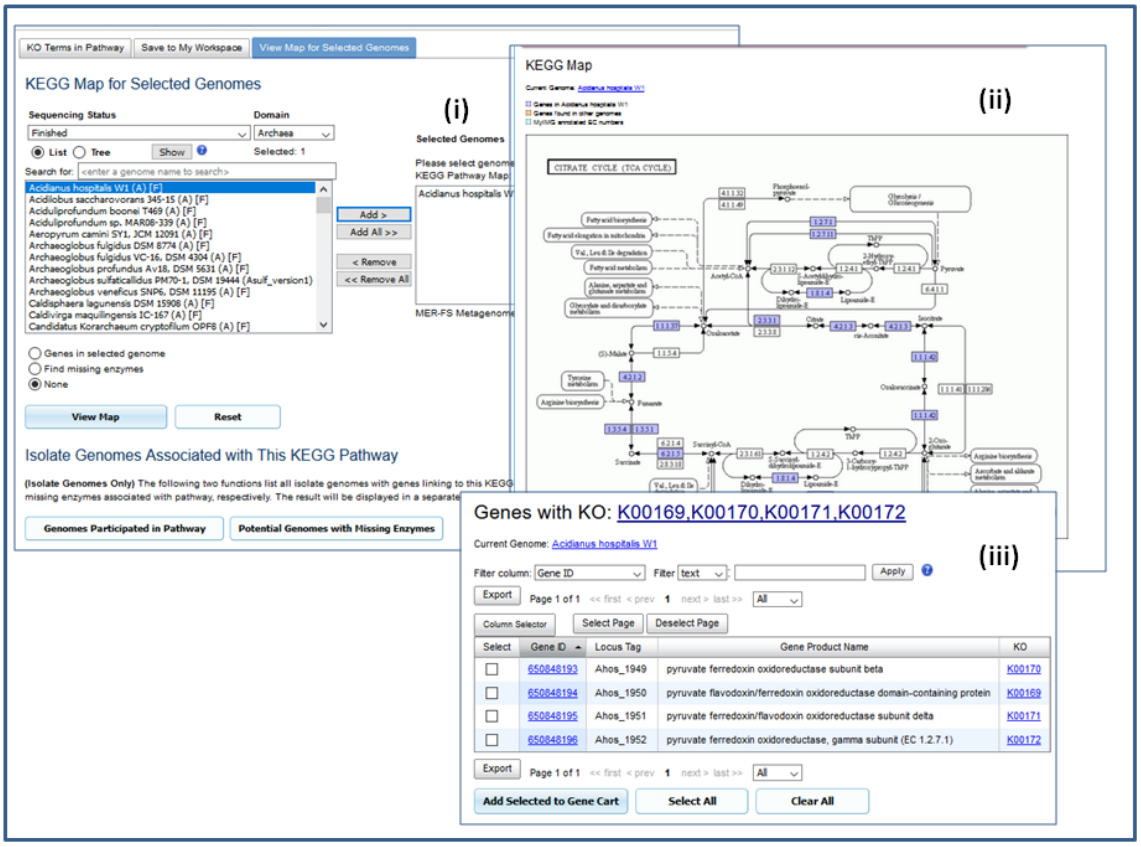

Figure 2. KEGG Map with Selected Genome.

There are two additional functions in the **KEGG Map for Selected Genomes** page (the two buttons in the lower part of Figure 2(i)):

- **Genomes Participated in Pathway**: The function lists all isolate genomes that have genes associated with KO term or enzymes in the pathway (Figure 3(i)). (Note that there is a limitation on numbers of genomes to be displayed.)
- **Potential Genomes with Missing Enzymes**: Since IMG uses higher cut-off values for gene to KO/enzyme association (see SOP for more details), there can be additional gene-enzyme associations that are not used in IMG gene function annotation. The function lists all isolate genomes having such "missing" associations (Figure 3(ii)). This is related to the finding missing enzymes function to be described below. (Note that there is a limitation on numbers of enzymes to be checked and a limitation on numbers of genomes to be displayed. Such limitations were set to avoid browser timeout.)

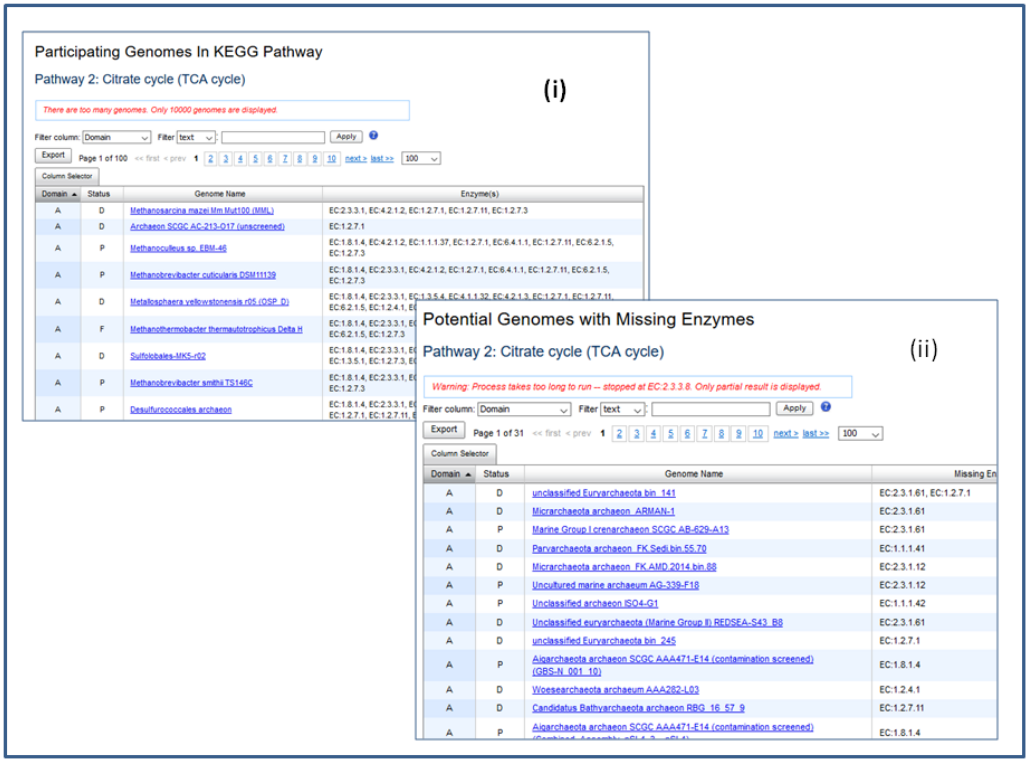

Figure 3. Participating Genomes in KEGG Pathway and Potential Genomes with Missing Enzymes.

For example, using the Potential Genomes with Missing Enzymes function described above, we find that *Halococcus agarilyticus 197A* may have missing enzyme annotations in KEGG Pathway *Styrene degradation*. So we select *Halococcus agarilyticus 197A* and select the "Find missing enzymes" option to view map (see Figure 4(i)). The KEGG map display in Figure 4(ii) shows two potential missing enzymes EC:3.5.5.1 and EC:3.5.1.4 (colored in light green). Selecting EC:3.5.1.4 and using homologs to *Halobacteria* we find 4 potential genes in *Halococcus agarilyticus 197A* that can be annotated with EC:3.5.1.4 (see Figure 4(iii)). Potential genes can be selected to add into the Gene Cart for further analysis. It is also possible to use MyIMG annotation feature to any of the 4 genes to add new gene-enzyme annotations. (See MyIMG User Guide for more detail on MyIMG annotations.)

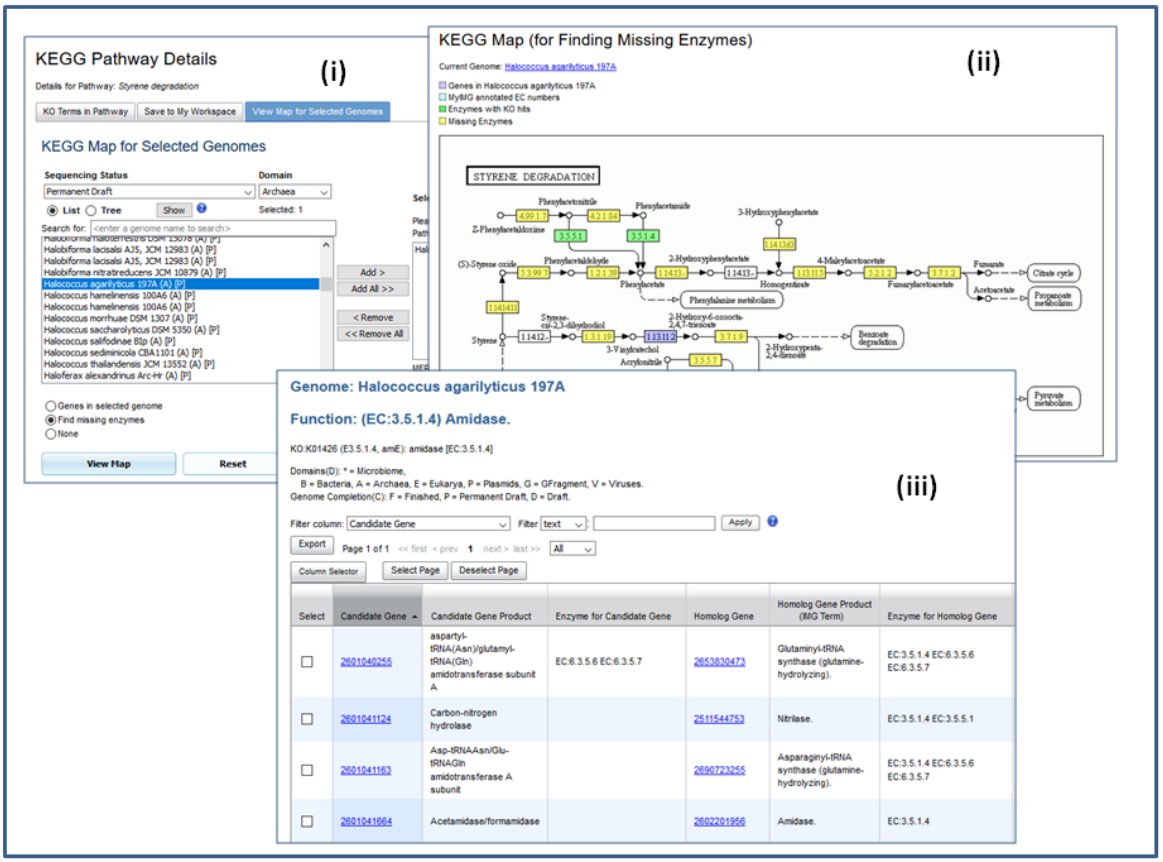

Figure 4. Finding Missing Enzymes.

KO List

IMG users can view and select all KO terms in IMG by selecting the **KO List** submenu under **KEGG** menu. **KO List w/ Stats** is similar to **KO List** except that each KO term is associated with (pre-computed) counts of isolate and metagenomes having genes annotated with this KO term (see Figure 5(i)). Users can select KO terms from the list to be added to the Function Cart for further analysis.

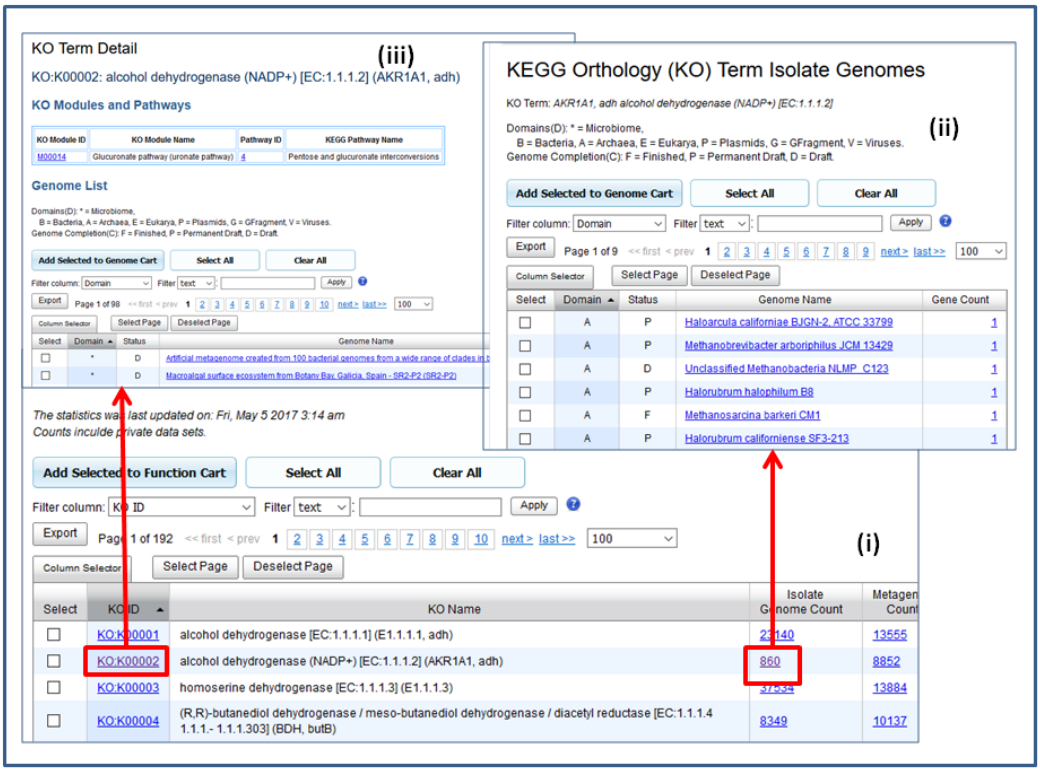

Figure 5. KO List and KO Term.

Clicking on a (meta)genome count will lead to a list of (meta)genomes having genes annotated with this KO term (see Figure 5(ii)). Genomes can be selected to add to Genome Cart for further analysis. Clicking on any gene count to view the actual gene list.

Clicking on a KO ID will lead to a KO Term Detail page showing KO Modules and Pathways, as well as genomes associated with the KO term (see Figure 5(iii)).

KEGG Module

IMG users can view and select all KEGG modules in IMG by selecting the **KEGG Module List** submenu under **KEGG** menu. **KEGG Module List w/ Stats** is similar to **KEGG Module List** except that each KEGG Module is associated with (pre-computed) counts of isolate and metagenomes having genes associated with this KEGG Module (see Figure 6(i)). KEGG Modules are not selectable for analysis.

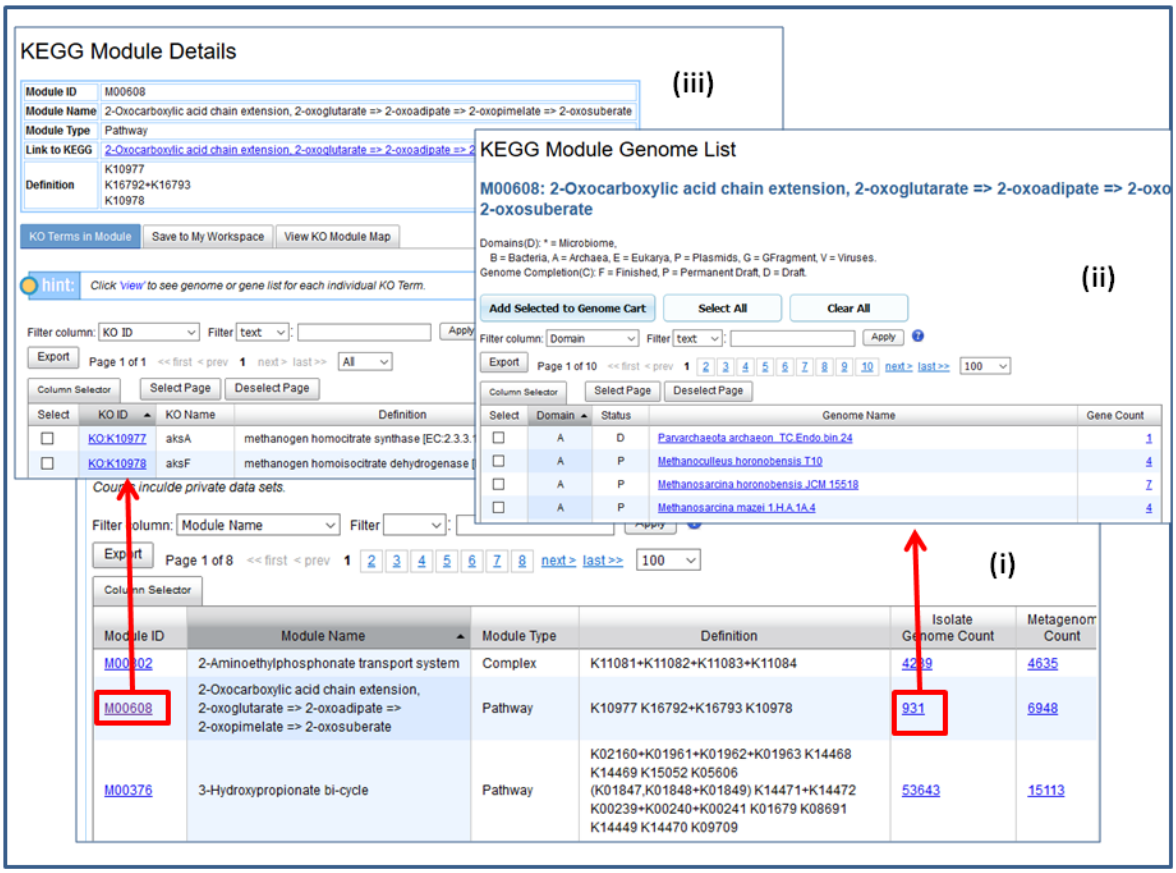

Figure 6. KEGG Modules.

Clicking on a (meta)genome count will lead to a list of (meta)genomes having genes associated with this KEGG Module (see Figure 6(ii)). Genomes can be selected to add to Genome Cart for further analysis. Clicking on any gene count to view the actual gene list.

Clicking on a Module ID will lead to a KEGG Module Details page showing KEGG Module definition and KO terms associated with the module (see Figure 6(iii)). Users can select KO terms to add to the Function Cart or to the Workspace (in the **Save to My Workspace** tab).

The **View KO Module Map** tab in the **KEGG Module Details** page (Figure 7(i)) allows user to select genomes to view on the Module Map. Click on the "Select Genome(s) to View on Map" button to perform genome selection as shown in Figure 7(ii). The "Show Map" button will lead to a colored KEGG Module Map with genomes mapped on KO terms in the module (Figure 7(iii)).

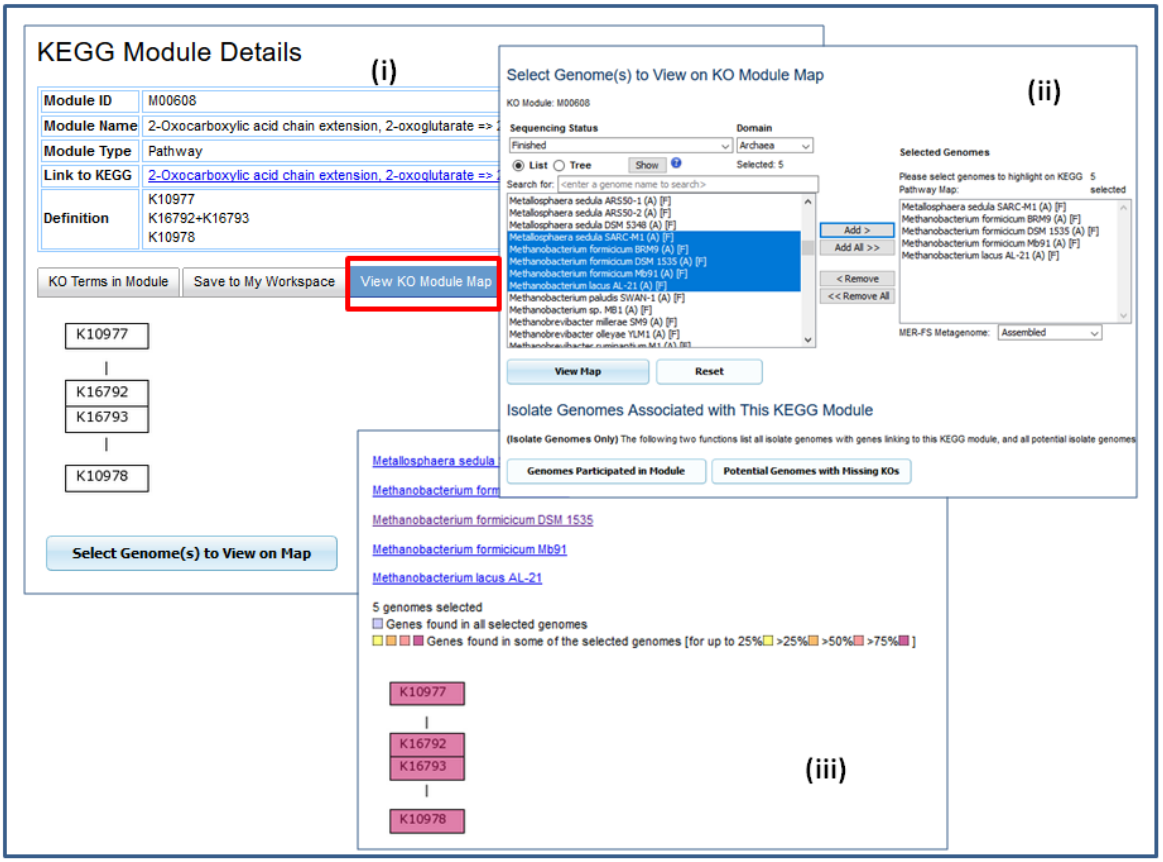

Figure 7. View Genomes on Selected KEGG Module Map.

There are also two additional functions "Genomes Participated in Module" and "Potential Genomes with Missing KOs." They are the corresponding functions of "Genomes Participated in Pathway" and "Potential Genomes with Missing Enzymes" in KEGG pathways as described above.

Orthology KO Terms

This submenu leads to the same KEGG Orthology (KO) Terms and Pathways page shown in Figure 1(i).

Pathways via KO Terms

This submenu leads to the same KEGG Orthology (KO) Terms and Pathways page shown in Figure 1(i) but with **KEGG Pathways via KO Terms** displayed.